# Guillain-Barré Syndrome in Military Populations

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# Notice

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  - The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.
- Research Ethics Statement
  - I declare no conflicts of interest or financial interests in any product or service mentioned in this article, including grants, employment, stock holdings, gifts, or honoraria.
  - All study results and data in this presentation met required research subject protection regulations.

# Recruits

- Navy at Great Lakes, IL
  - Increasing annual trend (0, 0, 2, 4, 6)
  - Increased use of EMR
- Marine Corps at Parris Island, SC
  - 3 cases over several years
  - 2 cases in January 2005
- ± Army and Air Force

# Guillain-Barré Syndrome (GBS)

## Objectives

- List current concepts from the literature
- Describe results of Navy studies on GBS
- List future steps

# The Syndrome

- Acute infective polyneuritis (autoimmune)
- Symmetric ascending paralysis
- Possible ventilator therapy

# Incidence

- Rare (cases per 100,000 [person-years])*
  - 0.4 - 1.5 in temperate climates
  - 0.8 in those under 18 years
  - 3.25 in those over 60 years
- Reported rates from various sources
  - 0.4 - 4 cases per 100,000 person-years

*__Cohen & Powderly: Infectious Diseases, 2nd ed.__, Copyright © 2004 Elsevier

# Conditions Associated with GBS

- Non-specific respiratory tract symptoms (50%)
- Campylobacter jejuni (26-40%)
- Mycoplasma pneumoniae
- Cytomegalovirus
- Epstein-Barr virus
- HIV-1
- Japanese encephalitis virus
- Hodgkin's disease
- Lymphoma
- Systemic lupus erythematosus
- Surgery
- Parturition
- Vaccines (<5%)
  - Vaccinia
  - Rabies
  - Influenza A/New Jersey/76
  - Oral poliovirus in Finland

# Other Notes

- Associations
  - Swine flu vaccine 1968 (OR = 6)
  - West Nile Virus
- Potential Biases
  - Estimates of rare conditions
  - Chart abstraction vs. electronic data
- Poisson vs. Normal statistical methods

# Questions

- Do military rates differ from literature?
- Are there sub-populations in the military with higher rates?
- Do rates differ between military services?

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# Studies

1. Case rate estimate
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    1. Feb 2005
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4. Line listing comparison
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# Poisson Regression

| Year | Count | At Risk | 95% Confidence Interval on Observed | | |
|---|---|---|---|---|---|
| | | | 95% LCL | Rate / 100k | 95% UCL |
| 2001 | 2 | 51,160 | 0.47 | 3.91 | 14.12 |
| 2002 | 4 | 43,777 | 2.49 | 9.14 | 23.39 |
| 2003 | 6 | 40,418 | 5.45 | 14.84 | 32.31 |

| Year | 1-sided p-values against reference rates | | | | | |
|---|---|---|---|---|---|---|
| Ref* | 0.4 | 0.8 | 1 | 2 | 4 | 8 |
| 2001 | **0.018** | 0.064 | 0.094 | 0.273 | 0.606 | 0.915 |
| 2002 | **<0.0001** | **0.0005** | **0.001** | **0.012** | 0.101 | 0.464 |
| 2003 | **<0.0001** | **<0.0001** | **<0.0001** | **0.0002** | **0.006** | 0.109 |

**Bolded values => statistically significant**

*multiple p-values are calculated using typical rates reported in the literature

Results derived from data from Zajdowicz, MJ, Feb 2004.

# “Statistically Significant” What are the causes?

- True difference
  - Apply existing scientific knowledge
- Artifact due to
  - Random error
    - Large sample size
    - Multiple well designed studies
  - Study bias
    - Identify and eliminate
  - Confounding
    - Identify and eliminate

# Review: VAERS 1990 – 2004*

- 14 year period
- Considered case if in any of 20 fields
- 171,506 records
- 149,542 (87.2%) with known onset date
  - Records with missing dates are similar to those with dates

*Derived from Sheets, J S 2004 Powerpoint

# VAERS Known onset date*

| n<br>Row % | GBS | Non-GBS | |
|---|---|---|---|
| Military | 37<br>0.52% | 7,013<br>99.48% | 7,050<br>100% |
| Non-Military | 769<br>0.54% | 141,723<br>99.46% | 142,492<br>100% |
| | 806 | 148,736 | 149,542 |

- OR = 1.02 (0.71 – 1.42)
- $\chi^2$ = 0.01 (p = 0.90 Fisher's Exact)
- No difference in reporting proportions

*Derived from Sheets, J S 2004 Powerpoint

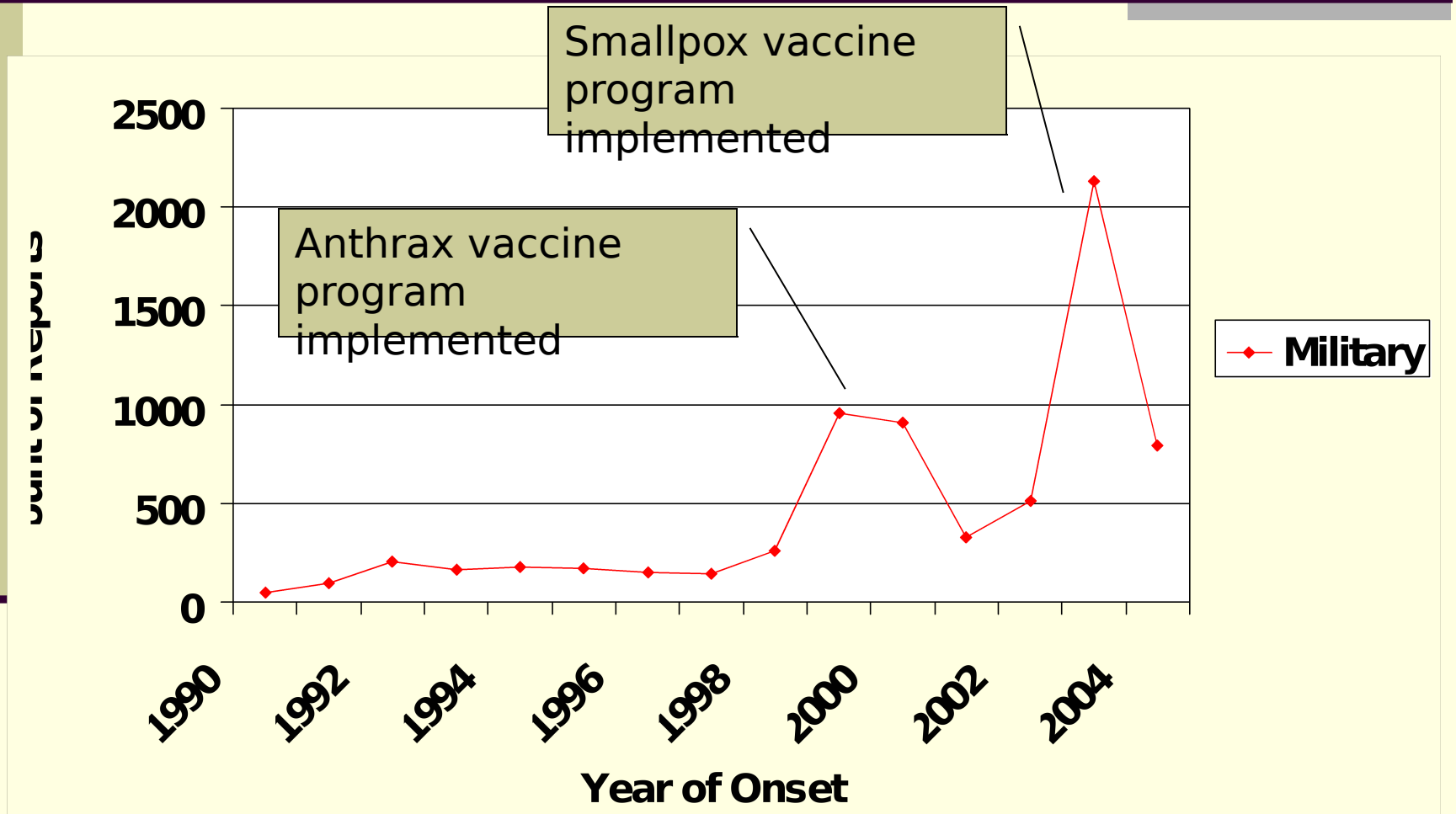
# VAERS Known onset date* 18-24 year old sub-analysis

| n<br>Row % | GBS | Non-GBS | |
|---|---|---|---|
| Military | 9<br>0.60% | 1,496<br>99.40% | 1,505<br>100% |
| Non-Military | 25<br>0.45% | 5,544<br>99.55% | 5,569<br>100% |
| | 34 | 7,040 | 7,074 |

- OR 1.33 (0.55 – 2.96)
- $\chi^2 = 0.55$ (p = 0.45, Fisher's Exact)
- No difference in reporting proportions

*Derived from Sheets, J S 2004 Powerpoint

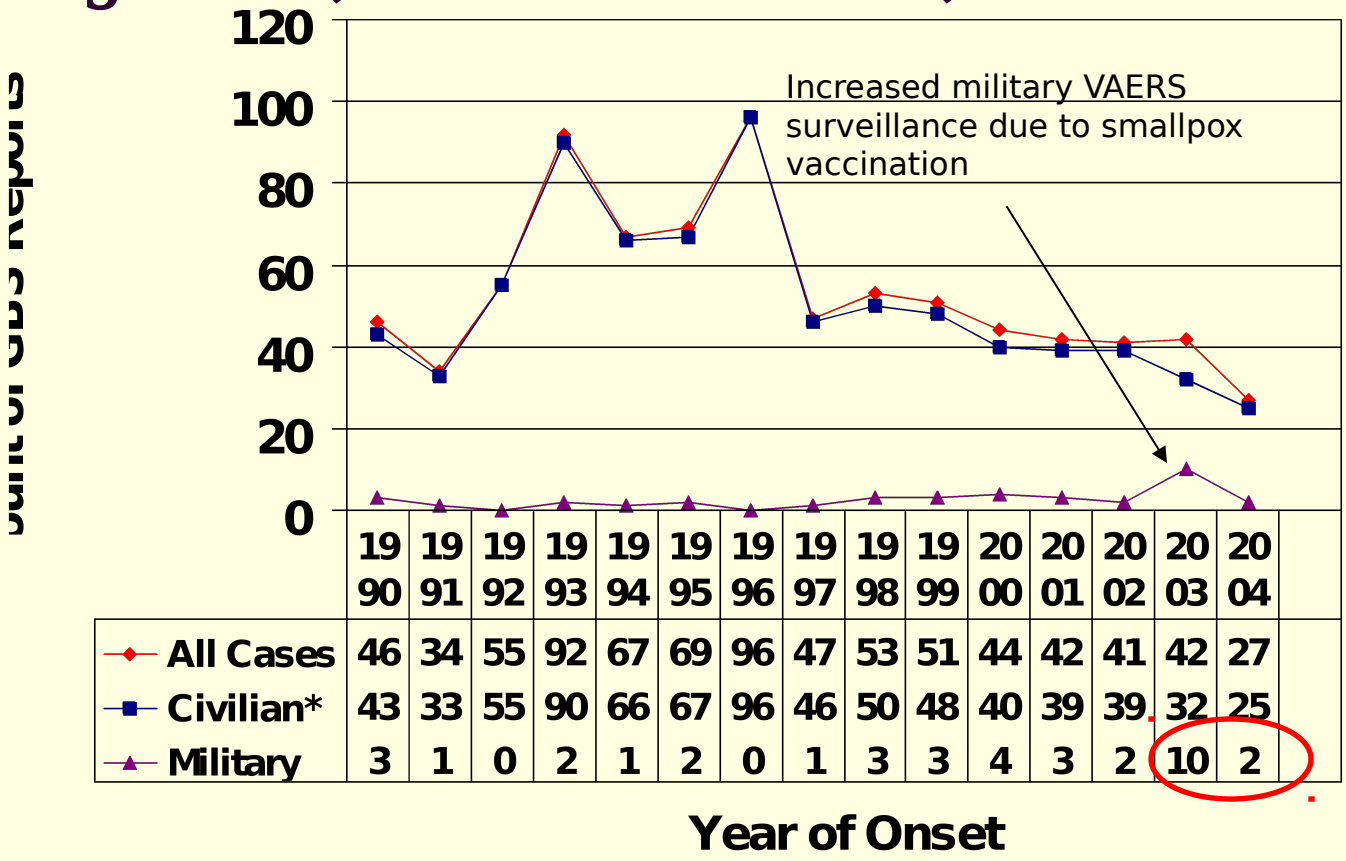
# All VAERS Reports-Military Jan 1,1990-Dec 31, 2004




*Derived from Sheets, S 2004 Powerpoint

All cases with a missing onset date or onset date prior to Jan 1, 1990 or after Dec. 31, 2004 were deleted

# GBS VAERS Reports by Onset Date
# Jan 1,1990-Dec 31, 2004




| | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| All Cases | 46 | 34 | 55 | 92 | 67 | 69 | 96 | 47 | 53 | 51 | 44 | 42 | 41 | 42 | 27 |
| Civilian* | 43 | 33 | 55 | 90 | 66 | 67 | 96 | 46 | 50 | 48 | 40 | 39 | 39 | 32 | 25 |
| Military | 3 | 1 | 0 | 2 | 1 | 2 | 0 | 1 | 3 | 3 | 4 | 3 | 2 | 10 | 2 |

*Cases with a missing value for either/both the Vaccine Administered by or the
Vaccine Funded by categories are included in the civilian category
All Cases with a missing onset date or onset date prior to 1990 were

# VAERS Summary

- No difference in proportionate reporting
- Counts only show difference in 2004
  - Indicator for recruits not available
- Low number of VAERS vs. GBS incidence
  - Poor reporting
  - Clinician attitude that GBS is not vaccine associated.

# Studies

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# M2 Inpatient

- Period
- Sources
- Numerators
- Populations

# M2 Studies

| Study Performed | Interval Start | Interval End | Included ICDs (Numerator) | Population Source |
|---|---|---|---|---|
| Feb 2005 | JAN 1999 | DEC 2004 | 357.0 | DMED |
| April 2005 | JAN 1999 | JAN 2005 | 357.0 & 357.9 | M2 Enrollment |

# M2 Preliminary Finding

- 6y1m period
- 158 first diagnoses recorded (Outpatient)
  - Concern that prevalent cases may be considered incident
  - Denominator data not available yet
  - Rates cannot be calculated until denominators available

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# NHRC Study

- Cox Proportional Hazards
- All AD
  - Period 1OCT1998 – 31MAR2004
  - 2,305,513 AD
  - 123 Excluded for prior diagnosis
  - 8,592,307 person-years
  - 314 incident cases (Crude 3.7/100k person-years)

# NHRC Study Method

- Identify “exposures”
  - Respiratory diagnoses
  - GI diagnoses
  - Other diagnoses
- Adjust for significant variables
  - e.g. age, sex, marital status, education
- Compare hazards between “exposure” groups.

# Disease Free Proportion by Respiratory Disease

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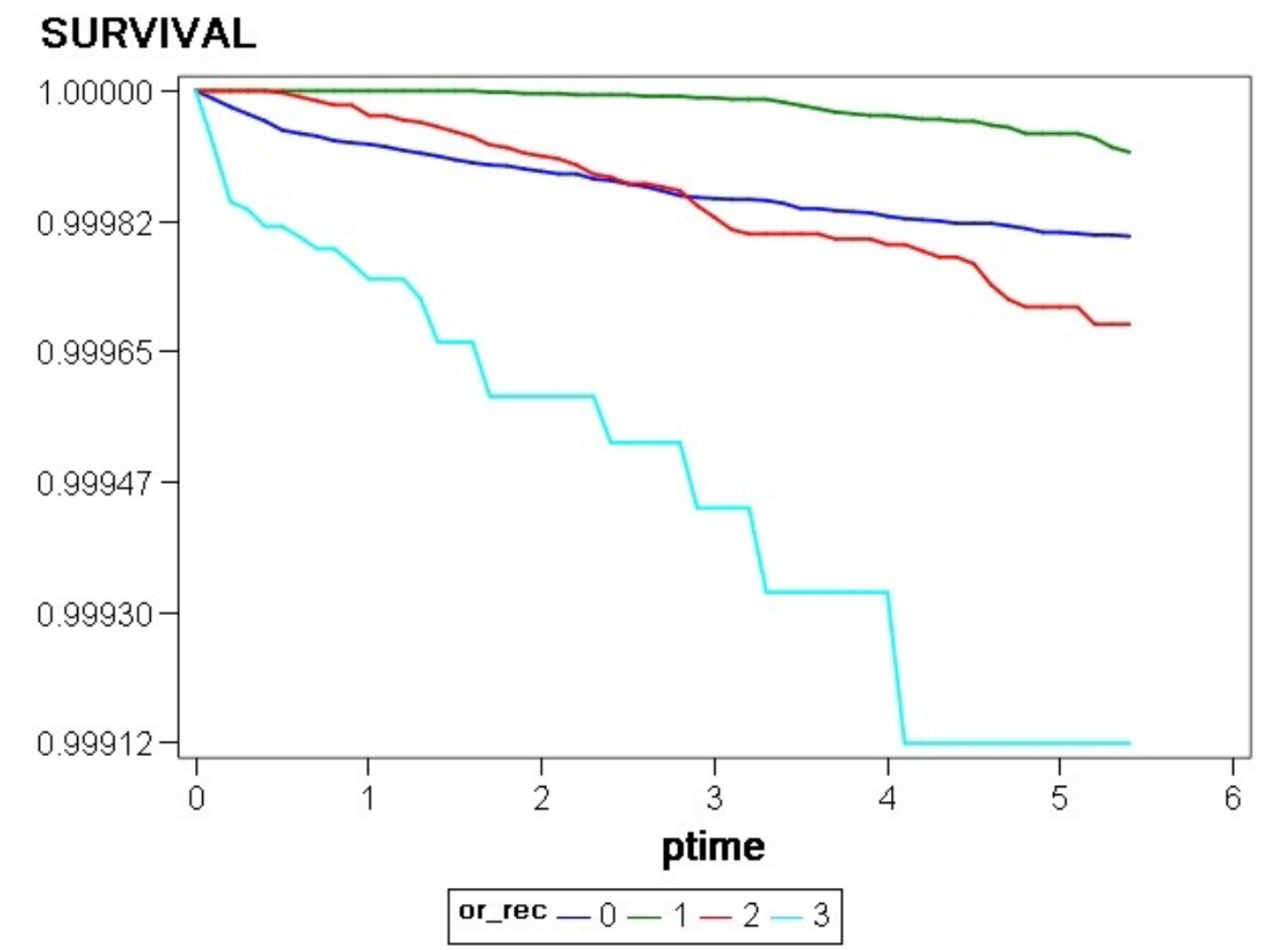

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# Epidemiologic Principles

- Care for those that are affected
- Implement effective prevention measures

- Epidemiology study steps
  - Determine denominators and rates for M2 study
  - Compare line listings to administrative data
- Advance knowledge where possible with well designed studies
  - Finish NHRC Cox Regression study

# Preventive Measures

- Expected benefit
  - Decrease respiratory infections
  - Decrease GI illness
- Uncertain benefit
  - Space immunizations out

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